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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,186	10/19/2000	Tan Thanh Dinh	ECV-5611	9184

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EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	**PAPER NUMBER**
1743	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

AS-11

Office Action Summary	Application No. 09/693,186	Applicant(s) DINH ET AL.	
	Examiner Maureen M. Wallenhorst	Art Unit 1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-19 and 21-24* is/are rejected.

7)☒ Claim(s) *9 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-6, 12-17 and 23-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Korte et al. (submitted in the Information Disclosure Statement filed on June 22, 2001).

Korte et al teach of a method for one-dimensional thin layer chromatography to separate phospholipids. In the method, a mixture of phospholipids such as phosphatidylcholine, phosphatidylethanolamine and phosphatidylinositol are extracted into a 2:1 extraction solvent of chloroform and methanol. The extraction solvent containing the phospholipids is then spotted onto a silica TLC plate, and placed into an elution solvent mixture. The TLC plate is developed in one direction, which allows for the separation of the phospholipids. The separated phospholipids are then visualized and detected. See pages 48-49 in Korte et al.

4. Claims 1-6, 12-17 and 23-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Entezami et al. (submitted in the Information Disclosure Statement filed June 22, 2001).

Entezami et al teach of a method for the analysis and separation of phospholipids by thin layer chromatography (TLC). In the method, a mixture of standard phospholipids such as sphingomyelin, phosphatidylcholine, phosphatidylethanolamine, etc are extracted into a volume of 2:1 chloroform and methanol. Spots of the extraction solvent containing the phospholipids are applied to a silica TLC plate, and then the plates are chromatographed in one direction in a TLC tank containing an elution solvent. Following development of the chromatogram, the individual phospholipids are scanned and detected. See pages 325-326 of Entezami et al.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 7-8 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Korte et al or Entezami et al in view of Schmitz et al (submitted in the Information Disclosure Statement filed on June 22, 2001). For a teaching of Korte et al and Entezami et al, see previous paragraphs in this Office action. Korte et al and Entezami et al fail to teach that the

elution solvent in the method for performing TLC contains chloroform, methanol, acetic acid and an aqueous solution of potassium chloride.

Schmitz et al teach of a method for the one-dimensional separation of phospholipids by thin layer chromatography (TLC). A mixture of phospholipids such as sphingomyelin, phosphatidylcholine and phosphatidylethanolamine are applied to a TLC plate, and separated in a one-step procedure using an elution solvent containing acetic acid, chloroform, methanol and potassium chloride in distilled water. See page 67 of Schmitz et al.

Based upon a combination of either Korte et al or Entezami et al with Schmitz et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the elution solvent containing chloroform, methanol, acetic acid and potassium chloride taught by Schmitz et al as the elution solvent in the TLC methods disclosed by Korte et al and Entezami et al since Schmitz et al teach that such an elution solvent in a TLC method serves to effectively separate several different types of phospholipids, which is the purpose of the methods taught by the primary references to Korte et al and Entezami et al., and is equivalent in function to the elution solvents disclosed in these primary references.

8. Claims 10-11 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Korte et al or Entezami et al in view of White et al (WO 99/50655). For a teaching of Korte et al and Entezami et al, see previous paragraphs in this Office action. Korte et al and Entezami et al fail to teach that the separated phospholipids are detected in an ultraviolet detection system after staining with primulin.

White et al teach of a method for separating target molecules such as an individual phospholipid from a mixture of phospholipids, that employs thin layer chromatography (TLC).

In one embodiment of the method, phosphatidylinositol is separated from a mixture containing the phosphatidylinositol and phosphatidylcholine by first extracting the phospholipids into an extraction solvent containing methanol and chloroform. Spots of the extraction solvent containing the phospholipids are then applied to a TLC silica plate. One-dimensional thin layer chromatography is then performed by the elution of a solvent in one direction. The separated phospholipid can then be detected by staining the phospholipid with primulin and exposing it to ultraviolet light. See claims 8-10 and 26 in White et al.

Based upon a combination of either Korte et al or Entezami et al with White et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to detect the separated phospholipids in the methods taught by Korte et al and Entezami et al by staining the separated phospholipids with primulin followed by exposure to ultraviolet light since White et al teach that this is one known way in which to detect and quantitate separated phospholipids, that is equivalent in function to the means for detection disclosed by Korte et al and Entezami et al.

9. Claims 9 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims since none of the prior art of record teaches or fairly suggests a method for separating phospholipids by one-dimensional thin layer chromatography, wherein the elution solvent in the method consists essentially of 35 parts chloroform, 10 parts methanol, 9.8 parts acetic acid and 1.2 parts of an aqueous solution of potassium chloride.

10. Applicant's arguments filed December 30, 2002 have been fully considered but they are not persuasive.

Applicants' arguments concerning the rejection of the claims under 35 USC 102 as being anticipated by the reference to White et al are persuasive, and therefore, this rejection has been withdrawn.

Applicants argue the rejection of the claims under 35 USC 102 as being anticipated by Korte et al by stating that the method of Korte et al results in overlapping analyte spots, and therefore, the method taught by Korte et al does not separate individual phospholipids so that each phospholipid can be individually detected, as recited in the instant claims. It is noted that this argument is not persuasive since in Korte et al, many of the same phospholipids separated in the instant invention (i.e. phosphatidylcholine, phosphatidylinositol, phosphatidylethanolamine) are also separated into discrete detectable spots on a TLC plate. See Figure 1 in Korte et al, which depicts separate identifiable spots for each phospholipid. In addition, the phospholipids in the method of Korte et al can be individually detected since Figure 3 in Korte et al identifies separate peaks for each phospholipid in the mixture analyzed. While the peaks may not be as clearly defined as in Figure 2 of the instant invention, nevertheless, the peaks in Figure 3 of Korte et al can be identified and assigned a particular phospholipid. Applicants' claims fail to define the degree of separation required between individual phospholipids or the required degree of delineation between peaks of the separated phospholipids.

Applicants argue the rejection of the claims under 35 USC 102 as being anticipated by Entezami et al by stating that the method of Entezami et al results in overlapping analyte spots, and therefore, the method taught by Entezami et al does not separate individual phospholipids so that each phospholipid can be individually detected, as recited in the instant claims. It is noted that this argument is not persuasive since in Entezami et al, many of the same phospholipids

separated in the instant invention (i.e. phosphatidylcholine, phosphatidylinositol, phosphatidylethanolamine) are also separated into discrete detectable spots on a TLC plate. See Figure 1 in Entezami et al, which depicts separate identifiable spots for each phospholipid. In addition, the phospholipids in the method of Entezami et al can be individually detected since Figure 1 in Entezami et al identifies separate peaks for each phospholipid in the mixture analyzed. While the peaks may not be as clearly defined as in Figure 2 of the instant invention, nevertheless, the peaks in Figure 1 of Entezami et al can be identified and assigned a particular phospholipid. Applicants' claims fail to define the degree of separation required between individual phospholipids or the required degree of delineation between peaks of the separated phospholipids.

Applicants argue the rejection of the claims under 35 USC 103 as being obvious over the combination of either Korte et al or Entezami et al with Schmitz et al by stating that the reference to Schmitz et al teaches away from the instant invention since Schmitz et al teach that a single TLC plate is inadequate to separate neutral phospholipids from a mixture of phospholipids. In response to this argument, it is first noted that the instant claims recite the separation of a mixture of phospholipids, and the recited phospholipids that are separated in one step using one TLC plate (i.e. phosphatidylcholine, phosphatidylinositol, phosphatidylethanolamine—see claim 2) are also separated in one step using one TLC plate in Schmitz et al. Schmitz et al teach that neutral lipids such as free cholesterol, triglycerides and cholesteryl esters must be separated on a different TLC plate from phospholipids such as phosphatidylcholine, phosphatidylinositol, and phosphatidylethanolamine. See Figures 1 and 3 in Schmitz et al. The instant claims do not encompass the separation of a mixture containing both phospholipids and the neutral lipids

described in Figure 1 of Schmitz et al using one TLC plate. Although two plates are used in Schmitz et al, one is used for separating a mixture of neutral lipids (i.e. free cholesterol, triglycerides and cholesteryl esters), while the other is used to separate the same mixture of phospholipids as separated in the instant invention.

Applicants also argue that the Examiner has not provided a reason as to why one skilled in the art would be motivated to combine the teachings of either Korte et al or Entezami et al with Schmitz et al. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, each of the references to Korte et al, Entezami et al and Schmitz et al teach of a method for separating a mixture of phospholipids using a single TLC plate in one direction, wherein the individual phospholipids in the mixture are resolved into discrete, detectable spots such that each individual phospholipid can be individually detected. See Figures 1 and 3 in Korte et al, Figure 1 in Entezami et al and Figure 3 in Schmitz et al. The secondary reference to Schmitz et al provides the motivation to use an elution solvent in the method taught by Korte et al and Entezami et al which contains chloroform, methanol, acetic acid and an aqueous solution of potassium chloride since Schmitz et al teach that such an elution solvent in a TLC method serves to effectively separate several different types of phospholipids, which is the purpose of the

methods taught by the primary references to Korte et al and Entezami et al., and is equivalent in function to the elution solvents disclosed in these primary references.

For all of the above reasons, Applicants' arguments are not found persuasive.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 703-308-3912. The examiner can normally be reached on Monday-Wednesday from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on (703) 308-4037. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9310.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

February 24, 2003

Maureen M. Wallenhorst
MAUREEN M. WALLENHORST
PRIMARY EXAMINER
GROUP [redacted] 1700